

Contemporary (2009-2014) clinical outcomes after femoro-popliteal bypass surgery for chronic limb threatening ischaemia are inferior to those reported in the UK Bypass versus Angioplasty for Severe Ischaemia of the Leg (BASIL) trial (1999-2004)

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1 **Contemporary (2009-2014) clinical outcomes after femoro-popliteal**
2 **bypass surgery for chronic limb threatening ischaemia (CLTI) are**
3 **inferior to those reported in the UK Bypass versus Angioplasty for**
4 **Severe Ischaemia of the Leg (BASIL) trial (1999-2004)**

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1 Abstract

2 **Introduction:** Bypass surgery (BS) remains the “gold standard” revascularisation strategy in
3 patients with chronic limb threatening ischaemia (CLTI) due to infra-inguinal disease. The
4 BASIL-1 trial showed that in CLTI patients who survived for 2 years or more, BS resulted in
5 better clinical outcomes. Despite this, there has been an increasing trend towards an
6 endovascular first approach to infra-inguinal CLTI. Our aim was to investigate whether
7 changes in practice have impacted upon the clinical outcomes of BS in our unit ten years
8 after BASIL-1.

9 **Methods:** Data for patients who underwent femoro-popliteal (FP) BS in BASIL-1 (1999-
10 2004) were retrieved from trial case record forms. The comparator contemporary series (CS)
11 comprised all patients undergoing FP BS for CLTI in our unit between 2009-2014.
12 Demographic and clinical outcome data on CS patients were collected from the
13 prospectively collected hospital electronic notes. Anatomic patterns of disease in the BASIL-
14 1 and CS cohorts were scored using Bollinger and GLASS. Statistical analysis was
15 performed in SAS v9.4.

16 **Results:** There were 128 BASIL-1 and 50 CS patients. Baseline age, gender, affected limb,
17 and diabetes prevalence were similar, as were days spent in hospital out to 12 months and
18 length of follow-up. BASIL-1 patients were more likely to be current smokers ($p=0.000$) and
19 had a higher creatinine ($p=0.04$). The 30-day morbidity and mortality were higher in BASIL-1
20 (45.3% vs 22%, $p=0.004$). There was no significant difference between BASIL-1 and CS with
21 regard to run-off Bollinger (37.7 v 32.1, $p=0.167$) and IP GLASS (0 vs 0, $p=0.390$) scores,
22 with both groups having a median of 2 run-off vessels. Amputation free survival (62% vs
23 28%, HR 1.86, 95%CI 1.18-2.93, $p=0.007$), limb salvage (85% vs 69%, HR 2.31, 95%CI
24 1.14-4.68, $p=0.02$), overall survival (69% vs 35%, HR 1.66, 95%CI 1.00-2.74, $p=0.05$) and
25 Major Adverse Limb Events (67% vs 47%, HR 1.93, 95%CI 1.15-3.22, $p=0.01$) were all
26 significantly better in BASIL-1.

27 **Conclusion:** Although 30-day mortality and morbidity were significantly lower, all of the
28 examined longer-term clinical outcomes after FP BS were significantly worse in the CS
29 group a decade on from BASIL-1. Further research in the form of prospective cohort studies
30 (PCS) and randomized controlled trials (RCT) is urgently required to determine if the CS
31 data reported here are generalizable to current vascular surgical practice and, if so, to
32 determine the reasons for these unexpected outcomes.

33

34

1 Introduction

2 Chronic limb threatening ischaemia (CLTI) is the most severe form of peripheral arterial
3 disease (PAD) and is characterized by ischemic rest pain and/or tissue loss/gangrene^{1,2}. The
4 worldwide incidence of CLTI is increasing due to ageing and the growing incidence of
5 diabetes mellitus and chronic kidney disease^{3,4}. Despite recent advances in medical
6 therapies and endovascular, surgical and hybrid revascularisation technologies and
7 techniques, CLTI patients remain at high risk of cardiovascular mortality and morbidity, and
8 limb loss⁵. With regard to evidence-based revascularisation (EBR), the first UK NIHR HTA-
9 funded Bypass versus Angioplasty for Severe Ischaemia of the Leg (BASIL-1) trial remains
10 the only published randomised controlled trial (RCT) to have compared a bypass surgery
11 (BS) first with a plain balloon angioplasty (PBA) first approach to infra-inguinal
12 revascularisation in CLTI⁶. BASIL-1 showed that in patients likely to live for more than two
13 years, overall (OS) and amputation free survival (AFS) were better following randomization
14 to BS than to PBA. Despite this 'level 1' evidence in favour of BS over PBA, there has been
15 a world-wide trend towards an endovascular first approach to the treatment of femoro-
16 popliteal (FP) disease in patients with CLTI. Those advocating such an approach point to
17 lower peri-procedural morbidity and mortality, and further claim that current best
18 endovascular treatment (BET) results in far superior outcomes than those reported in
19 BASIL⁷⁻⁹. Although not evidence-based, in many vascular units around the world, BS is
20 increasingly reserved for those patients who cannot have endovascular intervention or
21 where such intervention has failed. Due to the lack of published contemporary series (CS)
22 of BS for CLTI, the impact of such practice on outcomes following BS is unknown. The aim
23 of the present study, therefore, is to compare clinical outcomes following FP BS in a CS
24 (2009-2014) from a single UK academic vascular unit with those reported in the BASIL-1 trial
25 operated a decade earlier (1999-2004).

26

1 **Methods**

2 The BASIL-1 trial randomised 452 patients presenting with CLTI due to infra-inguinal
3 disease to either a BS-first or a PBA-first revascularisation strategy. The recruitment period
4 was 1999 to 2004 and follow up ended on 1 July 2007¹⁰. For the present analysis, the
5 BASIL-1 cohort comprised trial patients undergoing primary FP BS with any conduit. The CS
6 cohort comprised patients undergoing primary FP BS for CLTI with any conduit in our unit
7 between 2009 and 2014 and follow-up ended on 31 May 2017. Within the CS study period
8 (2009-2014), 132 FP BS were performed in our unit. Of these, 72 BS were for claudication
9 (IC) or popliteal aneurysm disease and so were excluded; as were four contralateral BS and
10 six secondary BS performed for failed endovascular interventions within the previous 12
11 months. This left 50 patients in the CS cohort undergoing primary FP BS for CLTI compared
12 with 128 BASIL-1 patients.

13 The BASIL-1 and CS cohorts were compared in terms of baseline factors, 30-day mortality
14 and morbidity, length of hospital stay out to 12 months and amputation-free survival (AFS),
15 limb salvage (LS), overall survival (OS), and freedom from re-intervention (FFR) and major
16 adverse limb events (MALE). FFR was defined as the absence of subsequent re-
17 vascularization or intervention for any post-operative complications. Minor amputations were
18 excluded as they were considered a consequence of the clinical presentation. Major
19 amputation was defined as amputation above the ankle joint. Minor amputation includes
20 amputation of single or multiple digits, or trans-metatarsal amputation (no Chopart's or
21 Lisfrank amputations were performed within the trial). MALE was defined as any ipsilateral
22 limb intervention (excluding minor amputation) after initial intervention. Bollinger¹¹ and Global
23 Vascular Guideline (GVG) GLASS grade and scores were used to quantify the pattern of
24 anatomical disease prior to intervention.

25 GLASS score is a new anatomical staging system designed by an expert global panel as
26 part of the Global Vascular Guidelines on Chronic Limb Threatening Ischaemia. GLASS is
27 part of the Patient, Limb, Anatomy paradigm presented in the GVG. GLASS involves
28 choosing the target artery pathway (TAP) for endovascular revascularisation from the origin
29 of the SFA (common and deep femoral disease are considered part of "inflow" and
30 considered corrected prior to more distal revascularisation) to the foot with the aim of
31 establishing in-line flow. Disease severity in FP and IP segments are graded separately on
32 features including length of disease, stenosis or occlusion and level of calcification. FP and
33 IP grades are combined within a matrix to determine GLASS stage. GLASS stage is
34 believed likely to correlate with endovascular immediate technical success rates and 12-

1 month limb-based patency (LBP) GLASS has been presented at the European Society of
2 Vascular Surgery, Lyon (France) 2017, and Society of Vascular Surgery VAM in San Diego
3 (2017) and Boston (2018). The concept is that GLASS will act as an aid to shared-decision
4 making and stratification within trials comparing different form of revascularisation. We
5 understand that the the GVG on CLTI are likely to be published in EJVES and JVS
6 supplement in Q4 of 2108.

7 Ethical approval was granted for the BASIL trial (ISRCTN – 45398889), no ethical approval
8 was required for the CS data collection as this is classed as audit of clinical outcomes.

9 Hazard ratios were used to detect statistically important differences in outcomes using 95%
10 confidence intervals. Differences between the cohorts were compared using t-test, chi-
11 squared and Wilcoxon Rank Sum tests according to distribution of data. Statistical analysis
12 was performed using SAS v 9.4.

13

1 Results

2 Patient age, gender, and prevalence of diabetes were similar in both cohorts. BASIL patients
3 were more likely to be current smokers, less likely to be on best medical therapy (BMT), and
4 had a higher baseline creatinine (**Table 1**). Immediate technical success rate, as judged by
5 the operating surgeon, was very high in both the BASIL-1 (126/128, 98%) and CS (50/50,
6 100%) cohorts. Minor amputation rates were equivalent between the two cohorts (23.4% vs
7 20%, $p=0.6$) suggesting equivalent burden of tissue loss. BASIL-1 trial patients had a non-
8 significantly longer mean (SD) index admission when compared to the CS patients (23.2
9 [26.3] vs 15.6 [20.3] days, $p = 0.7$). However, difference in cumulative inpatient hospital days
10 by 12 months had virtually disappeared (24.2 [26.4] versus 27.3 [26.8] days, $p = 0.5$).
11 BASIL-1 patients suffered significantly higher overall combined peri-operative (30-day)
12 mortality and morbidity (45% vs 22%; $p = 0.004$), including higher rates of wound infection
13 ($p=0.02$). However, there was no significant difference in major adverse cardiac events
14 (MACE) (8% vs 2%, $p=0.1$) (**Table 2**). With regard to long-term clinical outcomes, AFS (62%
15 vs 28%, HR 1.86, 95% CI 1.18-2.93, $p=0.007$), LS (85% vs 69%, HR 2.31, 95% CI 1.14-
16 4.68, $p=0.02$), OS (69% vs 35%, HR 1.66, 95% CI 1.00-2.74, $p=0.05$) and MALE (67% vs
17 47%, HR 1.93, 95% CI 1.15-3.22, $p=0.01$) were all significantly better in the BASIL-1 cohort
18 (**Figures 1-4**). FFR (76% vs 60%, HR=1.70, 95% CI 0.88 – 3.27, $p=0.1$) was non-
19 significantly better in BASIL-1 when compared to the CS cohort (**Figure 5**). In terms of
20 anatomic burden of disease, there was no significant difference between BASIL-1 and CS
21 with regard to run-off Bollinger score (37.7 vs 32.1, $p=0.167$) and IP GLASS (0 vs 0,
22 $p=0.390$) grade, with both groups having a median of 2 run-off vessels. Nor was there any
23 difference between total Bollinger score (63.1 vs 65.4, $p=0.926$). However, patients in the
24 CS had a significantly higher FP GLASS score (3 vs 4, $p=0.000$) (**Table 3**).

25

1 Discussion

2 In the present study, although peri-operative (30-day) mortality and morbidity were
3 significantly lower, long-term clinical outcomes following primary FP BS for CLTI in our unit
4 between 2009 and 2014 were significantly worse than those reported in the BASIL-1 trial a
5 decade earlier (1999-2004). Further research is required to determine if the CS data
6 reported here are generalizable to current vascular surgical practice and, if so, to determine
7 the reasons for these unexpected data. Possible causes include a loss of surgical skills as a
8 result of the overall reduction in open vascular procedures and/or a tendency to reserve BS
9 for patients considered unsuitable for endovascular intervention due the severity of their
10 tissue loss and/or the extent and complexity of their underlying disease¹²⁻¹⁵. While loss of
11 surgical skills is certainly possible, this does not appear to be supported by the observation
12 that CS patients had lower overall 30-day mortality and morbidity as well as a trend towards
13 a shorter index admission¹⁶⁻¹⁹. With regard to the clinical severity of disease, the proportion
14 of patients with tissue loss was similar in the two cohorts. We were unable to determine the
15 extent of tissue loss in the CS patients with same precision as was the case in BASIL-1.
16 However, using rates of minor amputation as a surrogate, it would seem that the severity of
17 tissue loss was broadly similar in both groups. With regard to anatomic complexity of
18 disease, the Bollinger scoring and GLASS grade would suggest a similar disease burden.
19 Importantly the run off scores were almost identical for both groups suggesting that the
20 outflow for bypass surgery was equivalent. Post procedural surveillance may have been
21 different between the two cohorts. Surveillance post bypass was not prescriptive in BASIL-
22 1, its use was not recorded and re-intervention was largely clinically driven. In the CS only
23 15 patients were enrolled in formal ultrasound graft surveillance, none had formal
24 haemodynamic surveillance. As such, it is possible that differences in post bypass care
25 could contribute to the difference in clinical outcomes observed.

26 An important question is the degree to which our practice and the outcomes reported here
27 can be generalized more widely to current vascular and endovascular practice within the UK
28 and elsewhere. Like many units, despite a lack of evidence indicating that endovascular
29 intervention offers a more clinically effective and cost-effective option for CLTI patients who
30 could have a vein bypass, and growing evidence that failed endovascular intervention
31 compromises outcomes following subsequent BS, we have increasingly employed an
32 endovascular first approach to the management of CLTI. Thus, during the study period
33 (2009-2014), almost five times more (n = 237) patients had a FP endovascular intervention
34 for CLTI than had BS (n = 50). In the UK, virtually all CLTI patients are managed within the
35 National Health Service (NHS), where care is provided free at the point of delivery to all UK

1 and European Union citizens, by salaried vascular surgeons and interventional radiologists.
2 As such, the “turf battles” and re-imburement issues seen elsewhere in the world are
3 largely irrelevant to UK practice. Rather, the main reason for our endovascular preference is
4 probably a reluctance to subject elderly and co-morbid patients to prolonged surgery and,
5 linked to that, a belief that an endovascular approach is associated with less resource
6 utilization in terms of operating theatre time and bed days in hospital. However, these beliefs
7 are not supported by hard data and we have to accept that our current practice may not be
8 maximizing long-term clinical outcomes for the greatest number of our CLTI patients.

9 Interestingly, in the UK, Heikkila et al.²⁰ have recently published 1-year outcomes following
10 lower limb revascularisation using data from the national vascular registry (NVR), hospital
11 episode statistics (HES), and the office of national statistics (ONS). The authors conclude
12 that overall survival and amputation rates have significantly improved over a 10-year period.
13 They suggest that one reason for the observed improvement may be centralization of
14 services due to increased specialization in vascular surgery. These UK national data would
15 seem to starkly contradict those reported here from a single UK academic vascular unit.
16 However, it must however be noted that Heikkila and colleagues grouped together a wide
17 range of surgical and endovascular procedures, studies patients with CLTI and intermittent
18 claudication (IC), and that their follow-up was short. Unfortunately, at the present time, there
19 are very few other published data with which we can compare our own long-term outcome
20 data. Thus, most surgical and endovascular CLTI cohorts reported in the literature have
21 limited follow-up and/or mix CLTI with IC and/or mix FP with infra-popliteal (IP) procedures
22 which makes interpretation of the data extremely difficult²¹⁻²³.

23 In summary, therefore, there is a clear and urgent need to perform further RCTs to
24 determine the pros and cons of a BET-first versus a BS-first revascularisation strategy in
25 sub-groups of CLTI patients presenting with different degrees of tissue loss and anatomic
26 complexities of disease. To this end, in the UK, NIHR HTA is funding the BASIL 2²⁴ and
27 BASIL 3²⁵ to inform practice in IP disease and the impact of drug eluting technologies in the
28 FP segment respectively. In the US, NIH have funded the BEST-CLI²⁶ trial. Together, these
29 on-going trials will report contemporary clinical outcomes in several thousand patients
30 undergoing BET and BS for CLTI and inform EBR decisions going forward.

31 **Conclusion**

32

33 Although 30-day mortality and morbidity were significantly lower, all of the examined longer-
34 term clinical outcomes after FP BS were significantly worse in the CS group a decade on
35 from BASIL-1.

1 **References**

- 2 1. Dormandy JA, Rutherford RB. Management of peripheral arterial disease
3 (PAD). TASC working Group. TransAtlantic Inter-Society Consensus (TASC).
4 J Vasc Surg. 2000;31 (1 pt 2):S1-S296
- 5 2. Anderseon JL, Halperin JL, Albert NM, Bozkurt B, Brindis RG, Curtis LH et al.
6 Management of patients with peripheral artery disease (compilation of 2005
7 and 2011 ACCF/AHA guideline recommendations): a report of the American
8 College of Cardiology Foundation/American Heart Association Task Force on
9 Practice Guidelines. Circulation. 2013;127:1425-1443
- 10 3. Sampson UK, Fowkes FG, McDermott MM, Criqui MH, Aboyans V, Norman
11 PE et al. Global and regional burden of death and disability from peripheral
12 artery disease: 21 world regions, 1990 to 2010. Glob Heart. 2014; 9: 145-158.
- 13 4. Fowkes FG, Rudan D, Rudan I, Aboyans V, Denenberg JO, Mc Dermott MM
14 et al. Comparison of global estimates of prevalence and risk factors for
15 peripheral artery disease in 2000 and 2010: a systematic review and analysis.
16 Lancet. 2013; 382: 1329-1340
- 17 5. Aikawa E, Nahrendorf M, Figueiredo JL, Swirski FK, Shtatland T, Kohler RH
18 et al. Osteogenesis associates with inflammation in early-stage
19 atherosclerosis evaluated by molecular imaging in vivo. Circulation 2007; 116:
20 2841-2850
- 21 6. Bradbury AW, Adam DJ, Bell J, Forbes JF, Fowkes FG, Gillespie I et al.
22 Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial: An
23 intention-to-treat analysis of amputation-free and overall survival in patients
24 randomized to a bypass surgery-first or a balloon angioplasty-first
25 revascularization strategy. J Vasc Surg. 2010 May;51(5 Suppl):5S-17S
- 26 7. Tsai TT, Rehring TF, Rogers RK, Shetterly SM, Wagner NM, Gupta R et al.
27 The Contemporary Safety and Effectiveness of Lower Extremity Bypass
28 Surgery and Peripheral Endovascular Interventions in the Treatment of
29 Symptomatic Peripheral Arterial Disease. Circulation. 2015; 132 (21); 1999-
30 2011

- 1 8. Bisdas T, Borowski M, Stavroulakis K, Torsello G; CRITISCH Collaborators.
2 Endovascular Therapy Versus Bypass Surgery as First-Line Treatment
3 Strategies for Critical Limb Ischemia: Results of the Interim Analysis of the
4 CRITISCH Registry. *JACC Cardiovasc Interv.* 2016 Dec 26;9(24):2557-2565.
- 5 9. Joels CS, York JW, Kalbaugh CA, Cull DL, Langan EM, Taylor SM. Surgical
6 implications of early failed endovascular intervention of the superficial femoral
7 artery. *J Vasc Surg.* 2008;47(3):562-565.
- 8 10. <https://www.journalslibrary.nihr.ac.uk/programmes/hta/960501/#/>
- 9 11. Bollinger A, Breddin K, Hess H, Heystraten FM, Kollath J, Konttila A et al.
10 Semiquantitative assessment of lower limb atherosclerosis from routine
11 angiographic images. *Atherosclerosis* 1981; 38:339.
- 12 12. Mills JL Sr, Conte MS, Armstrong DG, Pomposelli FB, Schanzer A, Sidawy
13 AN et al. Society for Vascular Surgery Lower Extremity Guidelines Committee.
14 The society for vascular surgery Lower Extremity Threatened Limb
15 Classification System: risk stratification based on wound, ischaemia, and foot
16 infection (WIfI). *J Vasc Surg.* 2014;59:220-34
- 17 13. Iida O, Takahara M, Soga Y, Kodama A, Terashi H, Azuma N. Three-Year
18 Outcomes of Surgical Versus Endovascular Revascularization for Critical
19 Limb Ischaemia. *Circ Cardiovasc Interv.*
- 20 14. Smith AD, Hawkins AT, Schaumeier MJ, de Vos MS, Conte MS, Nguyen LL.
21 Predictors of major amputation despite patent bypass grafts. *J Vasc Surg*
22 2016;63:1279-88.
- 23 15. Mehaffey JH, Hawkins RB, Fashandi A, Cherry KJ, Kern JA, Kron IL et al.
24 Lower extremity bypass for critical limb ischemia decreases major adverse
25 limb events with equivalent cardiac risk compared with endovascular
26 intervention. *J Vasc Surg* 2017;66:1109-16.
- 27 16. Moxey PW, Hofman D, Hinchliffe RJ, Poloniecki J, Loftus IM, Thompson MM,
28 et al. Volume-outcome relationships in lower extremity arterial bypass surgery.
29 *Ann Surg* 2012;256: 1102-7.
- 30 17. Holt PJE, Poloniecki JD, Loftus IM, Thompson MM. Meta- analysis and
31 systematic review of the relationship between hospital volume and outcome
32 following carotid endarterectomy. *Eur J Vasc Endovasc Surg* 2007;33:645-

1 51.

- 2 18. Marlow NE, Barraclough B, Collier NA, Dickinson IC, Fawcett J, Graham JC,
3 et al. Effect of hospital and surgeon volume on patient outcomes following
4 treatment of abdominal aortic aneurysms: a systematic review. *Eur J Vasc*
5 *Endovasc Surg* 2010;40:572-9.
- 6 19. Johnston LE, Tracci MC, Kern JA, Cherry KJ, Kron IL, Upchurch GR Jr et al.
7 Surgeon, not institution, case volume is associated with limb outcomes after
8 lower extremity bypass for critical limb ischemia in the Vascular Quality
9 Initiative. *Vasc Surg* 2017;66:1457-63.
- 10 20. Heikkila K, Mitchell DC, Loftus IM, Johal AS, Waton S, Cromwell DA.
11 Improving 1-year Outcomes of Infringuinal Limb Revascularisation: A
12 Population-Based Cohort Study of 104 000 Patients in England.
13 *Circulation*. 2018 Jan 9. doi: 10.1161/CIRCULATIONAHA.117.029834.
- 14 21. Popplewell MA, Davies HOB, Narayanswami, Renton M, Sharp A, Bate G et
15 al. A Comparison of Outcomes in Patients with Infrapopliteal Disease
16 Randomised to Vein Bypass or Plain Balloon Angioplasty in the Bypass
17 versus Angioplasty for Severe Limb Ischaemia of the Leg (BASIL) trial. *Eur J*
18 *Endovasc Surg*. 2017 Aug; 54(2):195-201.
- 19 22. Arhuidese I, Hicks CW, Locham S, Obeid T, Nejim B, Malas MB. Long-term
20 outcomes after autogenous versus synthetic lower extremity bypass in
21 patients on hemodialysis. *Surgery* 2017;162:1071-9.
- 22 23. Darling JD, McCallum JC, Soden PA, Korepta L, Guzman RJ, Wyers MC et al.
23 Results for primary bypass versus primary angioplasty/stent for lower
24 extremity chronic limb-threatening ischemia. *J Vasc Surg*. 2017;66(2):466-475
- 25 24. Popplewell MA, Davies H, Jarrett H, Bate G, Grant M, Patel S et al. Bypass
26 versus angioplasty in severe ischaemia of the leg - 2 (BASIL-2) trial: study
27 protocol for a randomised controlled trial. *Trials*. 2016;17(1):11.
28 doi:10.1186/s13063-015-1114-2.
- 29 25. Hunt BD, Popplewell MA, Davies H, Meecham L, Jarrett H, Bate G et al.
30 BALloon versus Stenting in severe Ischaemia of the Leg-3 (BASIL-3): study
31 protocol for a randomised controlled trial. *Trials*. 2017;18(1):224.

1 doi:10.1186/s13063-017-1968-6.

2 26. Menard MT, Farber A, Assmann SF, Choudhry NK, Conte MS, Creager MA et
3 al. Design and Rationale of the Best Endovascular Versus Best Surgical
4 Therapy for Patients With Critical Limb Ischemia (BEST-CLI) Trial. *J Am Heart*
5 *Assoc.* 2016;5(7):e003219. doi:10.1161/JAHA.116.003219.

6